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THE STATE OF L-CA^{2+} CHANNELS IN HYPERTENSIVE VESSELS

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Several reports suggest that altered Ca^{2+} handling is associated with the development of hypertension. Abnormalities of Ca^{2+} channels of vascular smooth muscle membrane in hypertension are suggested by the observation that arteries from hypertensive rats show increased sensitivity to the Ca^{2+} channel activator Bay K 8644 and even to the elevation of extracellular Ca^{2+} and show a higher affinity for PN-200110 binding. We have reported that abnormalities of Ca^{2+} channels in arteries from hypertensive animals and their lower membrane potential may be related to labile factors which could be vasoconstrictors such as endothelin-1.

We investigated the effect of BQ-123, an antagonist of the ET_A receptor, which has been reported to produce a significant decrease in blood pressure in stroke-prone spontaneously hypertensive rats and in transgenic renin hypertensive rats on the reactivity of SHR aorta to the Ca^{2+} channel activator Bay K 8644. BQ 123 (1 µM) decreased the sensitivity to Bay K 8644 of aortic rings of SHR down to that of WKY.

This result suggest that endothelin could be involved in the hyperreactivity of Ca^{2+} channels in SHR aorta. The effect of BQ-123 cannot be attributed to an interaction with the NO release since the experiments were performed in the presence of L-NNA. We have previously shown that threshold of subthreshold concentrations of endothelin-1, close to the physiological one, can potentiate the responses to vasoconstrictor agents and to Bay K 8644. Significant increase in the immunoreactive endothelin-1 content and in the pre-proendothelin-1 gene expression have been found in vessels from DOCA-salt hypertensive rats suggesting that endothelin could be increased in hypertension. Our observation of the specific action of an endothelin antagonist in isolated SHR aorta is in full agreement with a role of endothelin in the pathogenesis of hypertension. The question open is the mechanism by which the peptide could affect the state of Ca-channels in hypertensive arteries.

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EFFECTS OF ENDOTHELIN-1, BASIC FIBROBLAST GROWTH FACTOR AND ACTIVIN A ON MITOGENESIS AND MITOGEN-ACTIVATED PROTEIN KINASE IN SWISS 3T3 FIBROBLASTS

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Activins are members of a superfamily of peptides that includes the transforming growth factors ß, inhibins, bone morphogenic proteins, etc. They are implicated in the regulation of a variety of biological event including the cardiovascular development of embryo. We found that Swiss 3T3 fibroblasts express activin receptor abundantly. In an attempt to characterize the mitogenic action of activin A, we examined the effects of activin A as well as ET-1 and bFGF on the DNA synthesis and the MAP kinase activity, which is thought to play important roles for G0/G1-S transition. All the human recombinant activin A (10 nM), ET-1 (10 nM) and bFGF (5 ng/ml) potently stimulated the [^{3}H]thymidine incorporation into DNA. Although ET-1 and bFGF increased MAP kinase activity, activin A at 10 nM did not affect the kinase activity. Furthermore, ET-1 and bFGF, but not activin A did induce the phosphorylation of MAP kinase. These observation suggest that the activation of MAP kinase is not involved in the activin A-induced DNA synthesis.

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THE BIOCHEMICAL AND PHARMACOLOGICAL CHARACTERIZATION OF A 36 kDa-MICROFIBRIL-ASSOCIATED PROTEIN FROM BOVINE AORTA

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We have reported here the biochemical and pharmacological characterization of a newly identified microfibril-associated protein of 36 kDa (36 kDa-MAP) from bovine aorta. Using Ca^{2+}-dependent affinity chromatography on a synthetic compound (CKA-1303)-coupled Sepharose, we obtained pure form of 36 kDa-MAP. This compound should serve as useful tool for clarifying the physiological roles of 36 kDa-MAP. 36 kDa-MAP remains associated with the membrane fraction in the presence of Ca^{2+} and non-ionic detergents and is dissociated by EGTA. In addition, $^{45}Ca^{2+}$-autoradiography clearly indicated that 36 kDa-MAP binds Ca^{2+}. Calvasculin, a newly identified EF-hand protein, is present abundantly in bovine aorta. This protein bound with 36 kDa-MAP in a Ca^{2+}-dependent manner in vitro. A stoichiometry analysis showed that the 36 kDa-MAP bound 2.2 calvasculin eq/mol of protein. Solid-phase binding assay

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